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# Understanding the Approval Process for New Cancer Treatments

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## The FDA's Role



## One Example: Herceptin®

Before September 25, 1998, women with advanced breast cancer who wanted to take the drug Herceptin needed to enroll in a clinical trial. But after that date, they could obtain it through their doctors, like any other prescription drug. That's because Herceptin had received official approval from the U.S. Food and Drug Administration (FDA).

In the months leading up to approval, researchers had reported promising results from studies of women with advanced breast cancer whose tumor cells had extra copies of a protein called HER2. Herceptin is designed to target that protein and kill the cancer cells, leaving healthy cells alone. One group of researchers found that women who took the drug along with standard chemotherapy survived longer than those who recieved only the chemotherapy. Another group found that Herceptin alone could help some women whose cancer was not responding to chemotherapy.

**Related Pages**

Drug Information Summaries [1]
NCI's drug information summaries provide consumer-friendly information about certain drugs that are approved by the U.S. Food and Drug Administration (FDA) to treat cancer or conditions related to cancer.

Protecting Participants in Clinical Trials [2]
A collection of material about the ways in which clinical trials participants are protected before and during the conduct of a study.

A few months later, after carefully reviewing the results and weighing the benefits against the risks of side effects, the FDA approved the drug for use in women with HER2-positive, advanced breast cancer.

Approval is only one step in the process by which new treatments are developed. In fact, the FDA estimates that, on average, it takes 8.5 years to study and test a new drug before it can be approved for the general public. That includes early laboratory and animal testing, as well as the clinical trials that evaluate the treatment in humans. The FDA plays a key role at three main points in this process:

- Determining whether or not the benefits of a new treatment outweigh the risks.
- Once clinical trials begin, deciding whether or not they should continue, based on reports of the treatment's side effects and effectiveness against disease.
- When clinical trials are completed, deciding whether or not the treatment should be sold to the public and, if so, what claims the drug manufacturer can make and what the label should say about directions for use, side effects, and warnings.

To make these decisions, the FDA must review studies submitted by the drug's sponsor (which is usually the company that makes the drug), evaluate any reports of side effects or complications (called "adverse events") from preclinical studies and previous clinical trials, and review the adequacy of the chemistry and manufacturing.

This process is lengthy, but it is meant to ensure that only beneficial treatments with acceptable side effects will make their way into the hands of the public. At the same time, recent laws and streamlined procedures

**EXHIBIT A**

within the FDA have accelerated the approval of effective treatments, especially for serious illnesses such as cancer. In addition, specific provisions make some treatments available to patients with special needs even before the approval process is complete.

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### From Lab to Patient Care

By law, the FDA must review all test results for new treatments to ensure that products are safe and effective for specific uses. "Safe" does not mean that the treatment is free of possible adverse side effects; rather, it means that the potential benefits have been determined to outweigh any risks. The testing process begins long before the first person takes the treatment, with preliminary research and animal testing.

If a treatment proves promising in the lab, the drug company or sponsor must apply for FDA approval to test it in clinical trials with people. The application is called an Investigational New Drug (IND) application. For drugs and recombinant proteins (such as cytokines and monoclonal antibodies), sponsors submit the IND to the Center for Drug Evaluation and Research [3], or CDER (see chart [4]). For other biologics, including gene therapies and vaccines, sponsors submit the IND to the Center for Biologics Evaluation and Research [5] (CBER).

Once the IND is allowed to proceed by CDER or CBER, clinical trials can begin. If the treatment makes it through the clinical trials process - that is, if the studies show the treatment is safe and effective - the sponsor may submit to the FDA another application. For drugs, this is a New Drug Application (NDA); for biologics, it's a Biologics License Application (BLA). The application must include the following:

- The exact chemical makeup of the drug or biologic
- Results of animal studies
- Results of clinical trials
- How the drug or biologic is made, processed, and packaged
- Quality control standards

Once the FDA receives the NDA or BLA from the sponsor, the formal New Drug Application Review Process (see chart [6]) or Biologics/Product License Application Review Process begins.

For an overview of the entire drug approval process, see the CDER's visual representation of The New Drug Development Process [7]. For more information about the biologic approval process, see CBER's Frequently Asked Questions [8] Web page.

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### Speed versus Safety in the Approval Process

During the approval process, the FDA classifies as "priority" those treatments that offer significant medical advances over existing therapies. But even in non-priority cases, the FDA's goal is that no more than 10 months will pass between when a complete application is submitted and the FDA has finished its review, either approving the drug or biologic, or providing the sponsor with a complete list of the issues that need to be addressed.

The process is not always smooth, however. Sometimes the FDA requests (or the FDA's advisory panel recommends) additional research or data. Some new approvals have taken as little as 42 days from the time the last part of the BLA/NDA is received; other more difficult applications have spent years in the approval process.

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### Expert Advice

The FDA relies on a system of independent advisory committees, made up of professionals from outside the agency, for expert advice and guidance in making sound decisions about drug approval. Each committee

meets as needed to weigh available evidence and assess the safety, effectiveness, and appropriate use of products considered for approval. In addition, these committees provide advice about general criteria for evaluation and scientific issues not related to specific products. The Oncologic Drugs Advisory Committee (ODAC) meets regularly to provide expert advice on cancer-related treatments and preventive agents.

Each committee is composed of representatives from the the fields of research science and medical practice. At least one member on every advisory committee must represent the consumer perspective.

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### Final Approval

As the FDA looks at all the data submitted and the results of its own review, it applies two benchmark questions to each application:

- Do the results of well-controlled studies provide **substantial evidence of the treatment's effectiveness**?
- Do the results show **the product is safe** under the conditions of use in the proposed labeling? In this context, "safe" means that potential benefits have been determined to outweigh any risks.

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### Continued Vigilance

The FDA's responsibility for new medical treatments does not stop with final approval. The CDER's Office of Compliance tracks drugs after approval to make sure that drug makers comply with current standards and regulations. CDER's Office of Drug Marketing, Advertising, and Communication monitors new drug advertising to make sure it is truthful and complete. Biologics regulated by CBER are followed with the same vigilance after approval by the Office of Compliance and Biologics Quality as well as the Advertising and Promotional Labeling staff. And through a system called MedWatch [9], the FDA gets feedback from health professionals and consumers on how the new treatments are working, any adverse reactions, and potential problems in labeling and dosage.

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### Online FDA Resources

The following information from the FDA should help you better understand the drug approval process:

- The CDER Handbook [10]
- Vaccine Product Approval Process [11]
- From Test Tube to Patient: New Drug Development in the U.S. [12]
- Milestones in U.S. Food and Drug Law History [13]
- Drugs Approved for Use With Cancer [14]

## Glossary Terms

**chemotherapy** (KEE-moh-THAYR-uh-pee)

Treatment with drugs that kill cancer cells.

**clinical trial**

A type of research study that tests how well new medical approaches work in people. These studies test new methods of screening, prevention, diagnosis, or treatment of a disease. Also called a clinical study.

**cytokine** (SY-toh-kine)

A substance that is produced by cells of the immune system and can affect the immune response. Cytokines can also be produced in the laboratory by recombinant DNA technology and given to people to affect immune responses.

**gene therapy** (jeen THAYR-uh-pee)

Treatment that alters a gene. In studies of gene therapy for cancer, researchers are trying to improve the body's natural ability to fight the disease or to make the cancer cells more sensitive to other kinds of therapy.

**monoclonal antibody** (MAH-noh-KLOH-nul AN-tih-BAH-dee)

A type of protein made in the laboratory that can locate and bind to substances in the body, including tumor cells. There are many kinds of monoclonal antibodies. Each monoclonal antibody is made to find one substance. Monoclonal antibodies are being used to treat some types of cancer and are being studied in the treatment of other types. They can be used alone or to carry drugs, toxins, or radioactive materials directly to a tumor.

**preclinical study**

Research using animals to find out if a drug, procedure, or treatment is likely to be useful. Preclinical studies take place before any testing in humans is done.

**protein** (PRO-teen)

A molecule made up of amino acids that are needed for the body to function properly. Proteins are the basis of body structures such as skin and hair and of substances such as enzymes, cytokines, and antibodies.

**recombinant** (ree-KOM-bih-nunt)

In genetics, describes DNA, proteins, cells, or organisms that are made by combining genetic material from two different sources. Recombinant substances are made in the laboratory and are being studied in the treatment of cancer and for many other uses.

**side effect**

A problem that occurs when treatment affects healthy tissues or organs. Some common side effects of cancer treatment are fatigue, pain, nausea, vomiting, decreased blood cell counts, hair loss, and mouth sores.

**vaccine**

A substance or group of substances meant to cause the immune system to respond to a tumor or to microorganisms, such as bacteria or viruses. A vaccine can help the body recognize and destroy cancer cells or microorganisms.

## Table of Links

1 http://cancer.gov/cancertopics/druginfo/alphalist
2 http://cancer.gov/clinicaltrials/digestpage/protecting-participants
3 http://www.fda.gov/cder
4 http://www.fda.gov/cder/handbook/ind.htm
5 http://www.fda.gov/cber/index.html
6 http://www.fda.gov/cder/handbook/nda.htm

7 http://www.fda.gov/cder/handbook/develop.htm
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12 http://www.fda.gov/fdac/special/newdrug/ndd_toc.html
13 http://www.fda.gov/opacom/backgrounders/miles.html
14 http://www.fda.gov/cder/cancer/druglistframe.htm

# *The New Drug Development Process:*

## Steps from Test Tube to New Drug Application Review

Click any of the following boxes or words